

Approval Date: OCT 18 2004

FREEDOM OF INFORMATION SUMMARY
SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 135-906

COMPONENT E-H
(Testosterone Propionate and Estradiol Benzoate)

COMPONENT E-H with TYLAN
(Testosterone Propionate and Estradiol Benzoate with Tylosin)

This supplement provides for addition to the labeling of the statements “A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.” to the warning section and “Do not use in veal calves. Effectiveness and animal safety in veal calves have not been established.” immediately following the indications.

Sponsored by:

**Ivy Laboratories
Division of Ivy Animal Health, Inc.
8557 Bond Street
Overland Park, KS 66214**

FREEDOM OF INFORMATION SUMMARY

COMPONENT E-H and COMPONENT E-H with TYLAN Ear Implant for Heifers Weighing 400 Lbs or More

1. GENERAL INFORMATION:

- a. File Number: NADA 135-906
- b. Sponsor: Ivy Laboratories
Division of Ivy Animal Health, Inc.
8557 Bond Street
Overland Park, KS 66214
Drug Labeler Code: 021641
- c. Established Names: Testosterone Propionate and Estradiol Benzoate
Testosterone Propionate and Estradiol Benzoate
with Tylosin
- d. Propriety Names: COMPONENT E-H
COMPONENT E-H with TYLAN
- e. Dosage Form: Implantation (ear implant) as per 21 CFR 522.842
- f. How Supplied: COMPONENT E-H: Each box contains 5 foil
pouches each containing 1 cartridge belt with 20
cells. Each cartridge cell contains 1 implant dose.
Each dose consists of testosterone propionate USP
200 mg and estradiol benzoate 20 mg.
- COMPONENT E-H with TYLAN: Each box
contains 5 foil pouches each containing 1 cartridge
belt with 20 cells. Each cartridge cell contains 1
implant dose. Each dose consists of testosterone
propionate USP 200 mg and estradiol benzoate 20
mg with 29 mg tylosin tartrate as a local
antibacterial.
- g. How Dispensed: OTC

- h. Amount of Active Ingredients: COMPONENT E-H:
200 mg testosterone propionate.
20 mg estradiol benzoate.
- COMPONENT E-H with TYLAN:
200 mg testosterone propionate.
20 mg estradiol benzoate.
29 mg tylosin tartrate.
- i. Route of Administration: Subcutaneous implantation on the posterior aspect of
the middle one-third of the ear by means of an
implant gun.
- j. Species/Class: Heifers weighing 400 lbs or more
- k. Recommended Dosage: COMPONENT E-H: One implant containing 200
mg testosterone propionate and 20 mg estradiol
benzoate.
- COMPONENT E-H with TYLAN: One implant
containing 200 mg progesterone and 20 mg estradiol
benzoate with 29 mg tylosin tartrate.
- l. Pharmacological Category: Steroid hormones, antibacterial
- m. Indications: COMPONENT E-H and COMPONENT E-H with
TYLAN: For growth promotion and improved feed
efficiency.
- n. Effect of Supplement: This supplement provides for addition to the
labeling of the statements "A withdrawal period has
not been established for this product in pre-
ruminating calves. Do not use in calves to be
processed for veal." to the warning section and "Do
not use in veal calves. Effectiveness and animal
safety in veal calves have not been established."
immediately following the label indications.

2. DRUG EFFECTIVENESS:

No new effectiveness data are required for the approval of this supplement. The products' effectiveness has been established in the Freedom of Information (FOI) Summaries for the parent new animal drug applications for COMPONENT E-H and COMPONENT E-H with TYLAN (NADA 135906).

3. TARGET ANIMAL SAFETY:

No new target animal safety data are required for the approval of this supplement. The products' target animal safety has been established in the Freedom of Information (FOI) Summaries for the parent new animal drug applications for COMPONENT E-H and COMPONENT E-H with TYLAN (NADA 135906).

4. HUMAN SAFETY:

No new human food safety data are required for the approval of this supplement. The products' human food safety has been established in the Freedom of Information (FOI) Summaries for the parent new animal drug applications for COMPONENT E-H and COMPONENT E-H with TYLAN (NADA 135906).

5. AGENCY CONCLUSIONS:

The information submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514 of the implementing regulations providing for the addition to the labeling of the statements "A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal." to the warning section and "Do not use in veal calves. Effectiveness and animal safety in veal calves have not been established." immediately following the indications. The labeling is modified to conform to agency policy (69 FR 135 pages 42443-42444 dated July 15, 2004, and 69 FR 68 page 18594 dated April 8, 2004.)

The Center for Veterinary Medicine has concluded that, for these products, adequate directions for use by the layperson have been provided and the products will have over-the-counter (OTC) status. Label directions are accompanied by pictorial diagrams and detailed instruction in plain language. The drugs are not controlled substances. The products' status remains OTC. The labeling is adequate for the intended use and has sufficient warnings/statements to prevent illegal use in veal calves.

This approval does not qualify for marketing exclusivity under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act.

Under the Center's supplemental approval policy (21 CFR 514.106(b)(2)), this is a Category II change. The approval of this change is not expected to have any adverse effect on the safety or effectiveness of this new animal drug. Accordingly, this approval did not require a reevaluation of the safety and effectiveness data in the parent application.

COMPONENT E-H with TYLAN is under the following U.S. patent number:

<u>U.S. Patent Number</u>	<u>Date of Expiration</u>
5,874,098	May 28, 2017

6. ATTACHMENTS:

Facsimile Labeling is attached as indicated below:

COMPONENT E-H Carton Label
COMPONENT E-H Foil Pouch (Front)
COMPONENT E-H Foil Pouch (Back)
COMPONENT E-H Package Insert
COMPONENT E-H with TYLAN Carton Label
COMPONENT E-H with TYLAN Foil Pouch (Front)
COMPONENT E-H with TYLAN Foil Pouch (Back)
COMPONENT E-H with TYLAN Package Insert

Important: Read enclosed instruction brochure and follow directions.

Store at controlled room temperature — 15°-30°C (59°-86°F). DO NOT refrigerate — avoid excessive heat and humidity.

COMPONENT[®]
BRAND IMPLANTS

E-H
HEIFER IMPLANTS

testosterone propionate USP 200 mg
and estradiol benzoate 20 mg



COMPONENT E-H implants are recommended for use in heifers weighing 400 lbs. or more for growth promotion and improved feed efficiency.

Contents: Five Cartridges each containing 1 cartridge cell with 20 pellets (each cell dose cell contains 1 implant dose). Each dose consists of testosterone propionate USP 200 mg and estradiol benzoate 20 mg.

Dosage: Administer 1 implant cell/animal. See package insert for complete instructions. Do not use in veal calves.

† Based on U.S. Animal Health, Inc. NADA 148-974 Approval by FDA.

100 IMPLANTS



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WARNING: Not to be used in animals intended for subsequent breeding, or in dairy animals. Implant one dose — 8 pellets (entire contents of one cartridge cell) — in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed or human food.

A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

RESTRICTED DRUG — USE ONLY AS DIRECTED (CALIFORNIA) — FOR USE IN ANIMALS ONLY — NOT FOR HUMAN USE — KEEP OUT OF REACH OF CHILDREN

Caution: For use in Heifers only. Bulling, vaginal and rectal prolapse, udder development, ventral edema and elevated tail-heads have occasionally been reported in heifers implanted with testosterone propionate and estradiol benzoate.

Important: Read the enclosed instruction brochure. Use as illustrated with a CAREFUL CLEAN TECHNIQUE. Never take short cuts at the expense of CLEANLINESS.

Manufactured by a non-sterilizing process.

COMPONENT E-H with Tylan is covered by U.S. Patent No. 5,874,098
COMPONENT is a registered trademark of Ivy Animal Health, Inc.
Manufactured for VetLife by Ivy Laboratories • Overland Park, KS 66214, USA
VetLife and Ivy Laboratories are divisions of Ivy Animal Health, Inc.

01 02 03 05

HEIFER IMPLANTS
testosterone propionate USP 200 mg
and estradiol benzoate 20 mg

COMPONENT[®]

3.125"



1/4" Seal Area

9.5"

COMPONENT
BRAND IMPLANTS

E-H

testosterone propionate USP 200 mg
and estradiol benzoate 20 mg

HEIFER IMPLANTS



VetLife

TEAR HERE

COMPONENT E-H implants are recommended for use in heifers weighing 400 lbs. or more for growth promotion and improved feed efficiency.

Contains: One Cartridge Belt[†] of 20 implants sealed in a sanitary foil pouch.

Dosage: Administer 1 implant per animal. See package insert for detailed instructions. Do not use in veal calves.

Manufactured by a non-sterilizing process.

[†]Patented by Ivy Animal Health, Inc.

NADA 135-906 Approved by FDA
One 20-Dose Cartridge Belt

9.375"

TEAR HERE

WARNING: Not to be used in animals intended for subsequent breeding, or in dairy animals. Implant one dose — 8 pellets (entire contents of one cartridge cell) — in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed or human food.

A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

**RESTRICTED DRUG — USE ONLY AS DIRECTED (CALIFORNIA) — FOR USE IN ANIMALS ONLY —
NOT FOR HUMAN USE — KEEP OUT OF REACH OF CHILDREN**

CAUTION: For Heifer use only. Bulling, vaginal and rectal prolapse, udder development, ventral edema and elevated tail-heads have occasionally been reported in heifers implanted with testosterone propionate and estradiol benzoate.

IMPORTANT: Read the enclosed instruction brochure. Use as illustrated with a CAREFUL CLEAN TECHNIQUE. Never take short cuts at the expense of CLEANLINESS.

Store at controlled room temperature - 15°-30°C (59°-86°F).

DO NOT refrigerate - avoid excessive heat and humidity.

COMPONENT is a registered trademark of Ivy Animal Health, Inc.

Manufactured for VetLife by Ivy Laboratories • Overland Park, KS 66214, USA

VetLife and Ivy Laboratories are divisions of Ivy Animal Health, Inc.

01 02 02 05



EXP

LOT

BLACK

GENESIS 1999032

COMPONENT
BRAND IMPLANTS

VetLife
HEIFER IMPLANTS

E-H

testosterone propionate USP 200 mg and
estradiol benzoate 20 mg

20 dose CARTRIDGE BELT*

For use with COMPONENT One Gun***
For Use in Animals Only

Each CARTRIDGE BELT holds 20 doses of COMPONENT® E-H Implants. Each dose of 8 pellets contains a total of 200 mg testosterone propionate USP and 20 mg estradiol benzoate. COMPONENT® E-H Implants are recommended for use in heifers weighing 400 lbs or more for IMPROVED GROWTH PROMOTION AND FEED EFFICIENCY.

Do not use in veal calves. Effectiveness and animal safety in veal calves have not been established.

DOSAGE:

Administer 1 implant per animal according to the following instructions.

GENERAL INSTRUCTIONS:

Study the instructions which should be followed carefully at all times, avoiding short cuts. Skin infection can be avoided by properly preparing implant site and implanter. During fly season use fly repellent on implant site. One designated team member should always do the implanting. Cleanliness of hands and instruments is important at all times.

WARNING

Not to be used in animals intended for subsequent breeding, or in dairy animals. Implant one dose — 8 pellets (entire contents of one cartridge cell) — in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed or human food.

A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

RESTRICTED DRUG — USE ONLY AS DIRECTED (CALIFORNIA) —
FOR USE IN ANIMALS ONLY — NOT FOR HUMAN USE —
KEEP OUT OF REACH OF CHILDREN

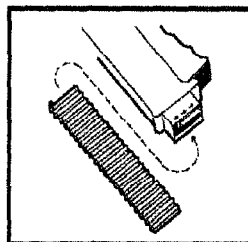
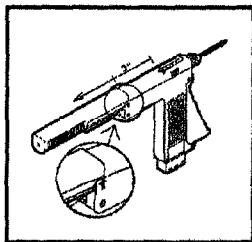
CAUTION:

For use in heifers only. Bulling, vaginal and rectal prolapse, udder development, ventral edema and elevated tail-heads have occasionally been reported in animals implanted with testosterone propionate and estradiol benzoate.

IMPLANTING INSTRUCTIONS:

Loading the Implanter

Load the implanter following the instructions supplied with each implanter.



Restrain the Animal

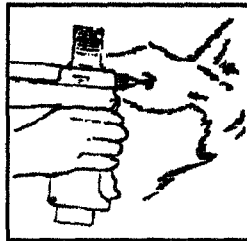
Speed of implantation as well as safety of handlers is best achieved by restraining animal in a squeeze chute using head restraint. When implanting horned cattle, better control is obtained with additional use of nose tongs.

**Prepare the Implant Site**

Scrub the back side of the ear (implant site) with a piece of clean absorbent cotton which has been soaked with a germicidal solution. Follow manufacturer's directions on germicide for correct strength and preparation of solution. Avoid getting disinfectant in animal's eyes.

**Where to Implant**

The full contents of one cartridge cell should be implanted beneath the skin on the back side of the middle one-third of the ear as illustrated in the drawing. The implant must not be closer to the head than the edge of the auricular cartilage ring farthest from the head. The location for insertion of the needle is a point toward the tip of the ear and at least a needle length away from the intended deposition site. Avoid injuring the large arteries, veins and cartilage of the ear.

**Insert the Needle**

With one hand firmly grasp the ear. With the other hand insert needle point through the skin and ease forward on a lateral plane until the entire length of the needle is under the skin.

Implant the Pellets

After inserting the needle fully in the correct implant position squeeze the trigger fully. As the needle is withdrawn from the ear, the controlled-pressure plunger action properly deposits the implant in the needle track. This procedure should prevent breakage or crushing of pellets if otherwise forced into contact with tough fibrous-tissue underlying the skin. The length and total contact area of a single dose are designed to permit absorption of the hormones after implantation to stimulate good weight gain. Broken or crushed pellets may interfere with rates of gain and may lead to undesirable side effects such as noted in the CAUTION.

Clean the Needle

Clean the implanter needle with alcohol or a properly diluted germicidal solution prior to implanting the next animal.

Storage Conditions

Store at controlled room temperature 15° to 30°C (59° to 86° F)
DO NOT refrigerate – avoid excessive heat and humidity.

Manufactured by a non-sterilizing process.

NADA 135-906, Approved by FDA

*U.S. Patent No. 4,531,938

**U.S. Patent Nos. 4,762,515 & 5,522,797 – Ivy Laboratories, Inc.

COMPONENT and COMPONENT One Gun are registered trademarks of Ivy Animal Health, Inc.

Manufactured for VetLife by Ivy Laboratories, Inc.
Overland Park, KS 66214, USA

VetLife and Ivy Laboratories are divisions of Ivy Animal Health, Inc.

Important: Read enclosed instruction brochure and follow directions.

Store at controlled room temperature – 15°-30°C (59°-86°F). DO NOT refrigerate – avoid excessive heat and humidity.

COMPONENT® E-H

BRAND IMPLANTS HEIFER IMPLANTS

with Tylan

testosterone propionate USP 200 mg and estradiol benzoate 20 mg
with 29 mg tylosin tartrate as a local antibacterial



COMPONENT E-H implants are recommended for use in heifers weighing 400 lbs. or more for growth promotion and improved feed efficiency.

Contents: 9 pellets each containing 1 car. cartridge with 3 car. cartridge pellets (1 testosterone propionate USP 200 mg and estradiol benzoate 20 mg and 29 mg tylosin tartrate as a local antibacterial).

Dosage: Administer 1 implant per animal. See package insert for detailed instructions. Do not use in heifers under 400 lbs.

Patented by Ivy Animal Health, Inc. NADA 138-936 Approved by FDA

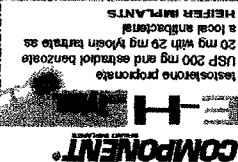
100 IMPLANTS



6 13562 04202 1



Use With Gray
Component
One Gun Only



WARNING: Not to be used in animals intended for subsequent breeding, or in dairy animals. Implant one dose — 9 pellets (entire contents of one cartridge cell) — in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed or human food.

A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

**RESTRICTED DRUG — USE ONLY AS DIRECTED (CALIFORNIA) — FOR USE IN ANIMALS ONLY —
NOT FOR HUMAN USE — KEEP OUT OF REACH OF CHILDREN**

Caution: For use in Heifers only. Bulling, vaginal and rectal prolapse, udder development, ventral edema and elevated tail-heads have occasionally been reported in heifers implanted with testosterone propionate and estradiol benzoate.

Important: Read the enclosed instruction brochure. Use as illustrated with a CAREFUL CLEAN TECHNIQUE. Never take short cuts at the expense of CLEANLINESS.

Manufactured by a non-sterilizing process.

COMPONENT E-H with Tylan is covered by U.S. Patent No. 5,874,008.
COMPONENT is a registered trademark of Ivy Animal Health, Inc.
Tylan is a registered trademark of Eli Lilly and Company
Manufactured for VetLife by Ivy Laboratories • Overland Park, KS 66214, USA
VetLife and Ivy Laboratories are divisions of Ivy Animal Health, Inc.

01 22 03 02

3.125"



1/4" Seal Area

9.5"

COMPONENT[®] E-H
BRAND IMPLANTS HEIFER IMPLANTS

testosterone propionate USP 200 mg and estradiol benzoate 20 mg
with 29 mg tylosin tartrate as a local antibacterial



VetLife[®]

TEAR HERE

COMPONENT E-H implants are recommended for use in heifers weighing 300 lbs. or more for growth promotion and improved feed efficiency.

Contains: One Cartridge Belt of 20 implants each sealed in a sanitary foil pouch. Each dose consists of testosterone propionate USP 200 mg and estradiol benzoate 20 mg with 29 mg tylosin tartrate as a local antibacterial.

Dosage: Administer 1 implant per animal. See package insert for detailed instructions. Do not use in veal calves.

Manufactured by a non-sterilizing process.

*Patented by Iry Animal Health, Inc. NADA 135-906. Approved by FDA



One 20-Dose Cartridge Belt

1 12.0/3

9.375"

TEAR HERE

WARNING: Not to be used in animals intended for subsequent breeding, or in dairy animals. Implant one dose — 9 pellets (entire contents of one cartridge cell) — in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed or human food.

A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

**RESTRICTED DRUG — USE ONLY AS DIRECTED (CALIFORNIA) — FOR USE IN ANIMALS ONLY —
NOT FOR HUMAN USE — KEEP OUT OF REACH OF CHILDREN**

Caution: For heifer use only. Bulling, vaginal and rectal prolapse, udder development, ventral edema and elevated tail-heads have occasionally been reported in heifers implanted with testosterone propionate and estradiol benzoate.

Important: Read the enclosed instruction brochure. Use as illustrated with a CAREFUL CLEAN TECHNIQUE. Never take short cuts at the expense of CLEANLINESS.

Store at controlled room temperature — 15°-30°C (59°-86°F).
DO NOT refrigerate — avoid excessive heat and humidity.

COMPONENT is a registered trademark of Ivy Animal Health, Inc.
Tylan is a registered trademark of Eli Lilly and Company.
Manufactured for VetLife by Ivy Laboratories • Overland Park, KS 66214, USA
VetLife and Ivy Laboratories are divisions of Ivy Animal Health, Inc.
01 22 02 02

PURCHASE SEAL 20 IMPLANTS



EXP

LOT

DATE

CONST. IMPRINT

COMPONENT®
BRAND IMPLANTS

VetLife

E-H WITH Tylan

HEIFER IMPLANTS

testosterone propionate USP 200 mg and
estradiol benzoate 20 mg with 29 mg tylosin
tartrate as a local antibacterial

20 dose CARTRIDGE BELT*

For use with the COMPONENT One Gun**
For Use in Animals Only

Each CARTRIDGE BELT holds 20 doses of COMPONENT® E-H implants. Each dose of 9 pellets consists of 8 pellets containing a total of 200 mg testosterone propionate USP and 20 mg estradiol benzoate plus 1 pellet containing 29 mg tylosin tartrate as a local antibacterial. COMPONENT® E-H Implants are recommended for use in heifers weighing 400 lbs or more for INCREASED RATE OF WEIGHT GAIN AND IMPROVED FEED EFFICIENCY.

Do not use in veal calves. Effectiveness and animal safety in veal calves have not been established.

DOSAGE:

Administer 1 implant per animal according to the following instructions.

GENERAL INSTRUCTIONS:

Study the instructions which should be followed carefully at all times, avoiding short cuts. Skin infection can be avoided by properly preparing implant site and implanter. During fly season use fly repellent on implant site. One designated team member should always do the implanting. Cleanliness of hands and instruments is important at all times.

WARNING

Not to be used in animals intended for subsequent breeding, or in dairy animals. Implant one dose — 9 pellets (entire contents of one cartridge cell) — in the ear subcutaneously. Any other site of implantation is in violation of Federal Law. DO NOT attempt to salvage implantation site for animal feed or human food.

A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

**RESTRICTED DRUG — USE ONLY AS DIRECTED (CALIFORNIA) —
FOR USE IN ANIMALS ONLY — NOT FOR HUMAN USE —
KEEP OUT OF REACH OF CHILDREN**

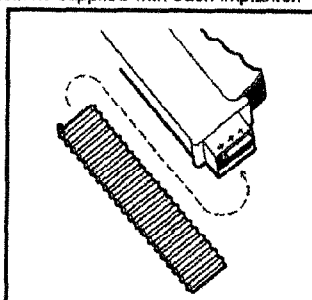
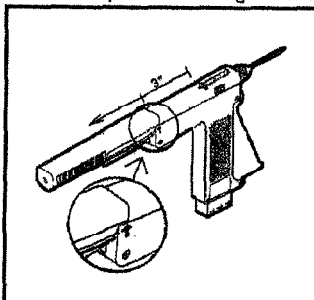
CAUTION:

For use in heifers only. Bulling, vaginal and rectal prolapse, udder development, ventral edema and elevated tail-heads have occasionally been reported in animals implanted with testosterone propionate and estradiol benzoate.

IMPLANTING INSTRUCTIONS:

Loading the Implanter

Load the implanter following the instructions supplied with each implanter.



Restrain the Animal

Speed of implantation as well as safety of handlers is best achieved by restraining animal in a squeeze chute using head restraint. When implanting horned cattle, better control is obtained with additional use of nose tongs.



Prepare the Implant Site

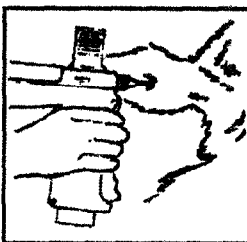
Scrub the back side of the ear (implant site) with a piece of clean absorbent cotton which has been soaked with a germicidal solution. Follow manufacturer's directions on germicide for correct strength and preparation of solution. Avoid getting disinfectant in animal's eyes.



Where to Implant

The full contents of one cartridge cell should be implanted beneath the skin on the back side of the middle one-third of the ear as illustrated in the drawing. The implant must not be closer to the head than the edge of the auricular cartilage ring farthest from the head. The location for insertion of the needle is a point toward the tip of the ear and at least a needle length away from the intended deposition site.

Avoid injuring the large arteries, veins and cartilage of the ear.



Insert the Needle

With one hand firmly grasp the ear. With the other hand insert needle point through the skin and ease forward on a lateral plane until the entire length of the needle is under the skin.

Implant the Pellets

After inserting the needle fully in the correct implant position squeeze the trigger fully. As the needle is withdrawn from the ear, the controlled-pressure plunger action properly deposits the implant in the needle track. This procedure should prevent breakage or crushing of pellets if otherwise forced into contact with tough fibrous-tissue underlying the skin. The length and total contact area of a single dose are designed to permit absorption of the hormones after implantation to stimulate good weight gain. Broken or crushed pellets may interfere with rates of gain and may lead to undesirable side effects such as noted in the CAUTION.

Clean the Needle

Clean the implanter needle with alcohol or a properly diluted germicidal solution prior to implanting the next animal.

Storage Conditions

Store at controlled room temperature 15° to 30°C (59° to 86° F)

DO NOT refrigerate - avoid excessive heat and humidity.

NADA 135-906, Approved by FDA

Manufactured by a non-sterilizing process.

*U.S. Patent No. 4,531,988

**U.S. Patent Nos. 4,762,515 & 5,522,797 - Ivy Animal Health, Inc.

COMPONENT E-H with Tylan is covered by U.S. Patent No. 5,874,098

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